

**REMARKS/ARUGMENTS**

Upon entry of this amendment, claims 1-9 will be canceled without prejudice or disclaimer of the subject matter recited therein. In this regard, Applicants have canceled the claims merely to expedite the prosecution of this application and preserve the right to contest the rejections set forth against these claims in the Final Office Action in one or more continuation applications in the event that the rejections are, in fact, repeated therein upon further consideration by the Examiner.

Moreover, claims 10, 12, 26, 28, 29, 31, 32 and 34 will be amended, whereby claims 10-34 will remain pending. Claims 10 and 16 are independent claims.

Claim 10 has been amended herein to include the description of the amount of the bonded antibody as being "0.5 to 4.5 mg per 100 mg of total lipids that constitute the liposome" instead of "0.1 to 2 mol% based on one mole of the maleimidated lipids contained in the liposome". Support for this amendment can be found in Applicants' originally filed specification, such as, for example, at page 10, last three lines to page 11, first two lines, wherein it is disclosed that, "For example, thiolated antibodies in an amount of 0.1 mole% (specifically, 0.17 mole%) to about 2 mole% (specifically, 1.5 mole%, 1.8 mole%), preferably 0.4 to 0.7 mole%, can be reacted with one mole of the maleimide groups (maleimidated lipids) so that 0.5 to 5.3 mg, 0.5 to 4.5 mg, preferably 1.2 to 2 mg, of antibodies are bonded per 100 mg of total lipids constituting the liposome."

Moreover, claims 11 and 16 have been amended to recite "1.2 to 2 mg per 100 mg of total lipids that constitute the liposome" in accordance with at least the above-noted disclosure in the originally filed application.

Still further, claims have been amended to change claim dependencies in view of claim cancellation, and to address the indefiniteness rejection as will be discussed below.

Reconsideration and allowance of the application are respectfully requested.

### **Discussion Of Telephone Conversations With The Examiner**

Applicants express appreciation for the courtesies extended by the Examiner to Applicants' representative Arnold Turk during a March 25, 2004 telephone conversation. During the telephone conversation, the new matter rejection was briefly discussed and the Examiner was reminded that during a December 11, 2003 personal interview at the Patent and Trademark Office the Examiner had indicated that the claim language would be acceptable. Applicants' representative indicated that the Final Office Action inappropriately included a new matter rejection without providing any explanation therein as to the basis of the rejection. The Examiner indicated that arguments should be presented, and the rejection would be reconsidered.

Moreover, Applicants note that a telephone interview was attempted in order to discuss the instant response prior to filing. The Examiner indicated that he was busy, but would have some time during the afternoon of June 15, 2004. A telephone call was made to the Examiner; however, the Examiner could not be reached. Accordingly, Applicants respectfully request that the Examiner contact the undersigned to discuss the application in the event that the Examiner does not deem the application to be in condition for allowance.

**Consideration Of Disclosure Statements And Documents Cited In International Search Report**

Applicants express appreciation for the inclusion with the Final Office Action of initialed copies of the Forms PTO-1449 submitted with the January 25, 2002 Information Disclosure Statement, whereby the Examiner's consideration of each of the documents listed thereon is of record.

Upon review of the disclosure statements, the Office Actions and the Notification of Acceptance of Application Under 35 U.S.C. 371 and 37 C.F.R. 1.494 and 1.495, Applicants note that two documents cited in the International Search Report have not been indicated to have been considered by the Examiner. In particular, EP 526700 A and Biochemistry, 36, (1), 66-75 are listed in the International Search Report, but have not been confirmed as being considered by the Examiner. In this regard, Applicants remind the Examiner that the Examiner will consider the documents cited in the International Search Report in a PCT national stage application when the Form PCT/DO/EO/903 indicates that both the International Search Report and the copies of the documents are present in the national stage file. In such a case, the Examiner should consider the documents from the International Search Report and indicate by a statement in the first Office Action that the information has been considered.

In the instant case, the Examiner has not indicated in the first Office Action that the documents have been considered. Therefore, in order that the record is clear with respect to the Examiner's consideration of the documents, Applicants are enclosing a completed Form PTO-1449 listing these two documents. The Examiner is therefore respectfully requested to

confirm the required consideration of these documents in this national stage application by forwarding an initialed copy of the form with the next communication from the Patent and Trademark Office.

To assist the Examiner's confirmation of consideration of these documents, Applicants are enclosing a copies of the documents. Moreover, Applicants note that EP 526700 A is a family member of U.S. Patent No. 5,264,221, which is being utilized in the rejection of the claims in the instant application.

#### **Request For Withdrawal Of Finality Of Office Action**

Applicants respectfully submit that the basis for the present rejection under 35 U.S.C. 112, second paragraph, that is included in the Final Office Action was not due to Applicants' amendment. While Applicants submit that the rejection is without appropriate basis and are amending the claims herein merely to advance prosecution of the application, Applicants respectfully submit that the rejection could have been made on the claims that were pending when the first Office Action was mailed.

The Examiner is reminded that, under present Patent and Trademark Office practice, an Office Action should not be made final where the examiner introduces a new ground of rejection therein that is neither necessitated by Applicants' amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p). In the instant situation, Applicants' amendment merely made a cosmetic change to claims 26-28 to clarify that the medicament is a

medicament composition and that use comprises administering to a patient. Certainly, neither the amendment to claim 26 nor the amendment to claim 28 necessitated the new ground of rejection.

**Accordingly, the finality of the Office Action is premature, and should be withdrawn in the event that the application is not allowed in response to the instant response.**

### **Claim Of Priority**

Applicants **once again** note that this application claims priority of Japanese Application Nos. 11-115737, filed April 23, 1999, and 11-115738, filed April 23, 1999. In this regard, a copy of the Form PCT/IB/304 was submitted with the papers when entering the national stage. **The Examiner is therefore respectfully requested to acknowledge the claim of foreign priority in the next communication from the Patent and Trademark Office as well as receipt of the certified copies of the priority documents in this national stage application.**

### **Response To Rejection Under 35 U.S.C. 112, First Paragraph**

Claims 1-9 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner asserts that the newly added limitation of 40 mole% does not have support in the originally filed application and therefore is deemed to be new matter.

In response, Applicants respectfully submit that this ground of rejection is without appropriate basis in that the rejection is silent as to any support as to why the language constitutes new matter.

In any event, as noted above, Applicants have canceled claims 1-9 to expedite the prosecution of this application. Applicants preserve the right to contest the rejections set forth against these claims in the Final Office Action in one or more continuation applications in the event that the rejections are, in fact, repeated therein upon further consideration by the Examiner.

Accordingly, this ground of rejection is no longer applicable in the instant application, and therefore should be withdrawn.

#### **Response To Rejection Under 35U.S.C. 112, Second Paragraph**

Claims 26-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that the rejection asserts that these methods of treatment cancer claims depend on composition either in claim 1 or 10, and that the parent claims do not recite any anti-cancer agents.

Initially, Applicants note that the rejected claimed are directed to compositions as well as methods and that the parent claims are directed to liposomes.

Moreover, it is clear that the compositions and methods of the rejected claims include medicaments therein to treat cancer. However, in order to advance prosecution of the application, the claims have been amended herein to even further clarify that the compositions and methods include medicaments for the treatment of cancer.

Accordingly, the rejection should be withdrawn.

**Response To Rejections Based Upon Prior Art**

In response to the rejection of claims 1-34 under 35 U.S.C. 102(b) as being anticipated by Tagawa, U.S. Patent No. 5,264,221, and under 35 U.S.C 103(a) as being unpatentable over Tagawa, Applicants respectfully submit the following.

Applicants note that independent claim 10 is directed to a liposome wherein an antibody is bonded through a thioether group to a liposome comprising lipids whose partial component has maleimidated terminal, and wherein an amount of the bonded antibody is 0.5 to 4.5 mg per 100 mg of total lipids that constitute the liposome.

Moreover, Applicants' independent claim 16 is directed to a liposome wherein a compound containing a polyalkylene glycol moiety and an antibody are bonded through thioether groups to a liposome comprising lipids whose partial component has maleimidated terminal, and wherein an amount of the bonded compound is 15 to 30 mole% and an amount of the bonded antibody is 1.2 to 2 mg per 100 mg of total lipids that constitute the liposome.

The Examiner is once again reminded that Applicants' specification, beginning at page 1, "Background Art" section, beginning in the second paragraph, discusses and contrasts Japanese Patent Unexamined Publication (Kokai) No. 4-346918 (hereinafter "JP '918") with the invention that is disclosed and claimed in the instant application. The Examiner is reminded that Tagawa is a family member of JP '918, and this family relationship between Tagawa and JP '918 is set forth in the Information Disclosure Statement, filed January 25, 2002. Despite the family relationship that has been presented on the record, the rejection neither indicates such relationship, nor does the rejection address any of the discussion of JP '918 in Applicants' specification.

Still further, it is once again noted that Tagawa includes overlapping inventors with the present application, in that the inventors named in Tagawa include, amongst other co-inventors, Toshiaki Tagawa and Saiko Hosokawa, who are the inventors of the presently claimed invention. Accordingly, Applicants have, by the present invention, provided improvements over prior art of which they were co-inventors.

Applicants note that Tagawa discloses the use of a thiolated antibody in a ratio of 0.1 mol% to 20 mol% based on 1 mol of maleimide group (column 4, lines 9 to 7 from the bottom). Also, Tagawa discloses in Example 3, a PEG modified liposome bound with an antibody. As explained in Example 3 of Tagawa, the liposome disclosed in Example 3 was prepared according to the method described in Example 2, which means that 100 mg of lipid was used for preparation of the liposome of Example 3. Moreover, in contrast to the liposomes recited in Applicants' claims, **Tagawa discloses in Example 2 (at column 7, lines 43-44) the preparation of a liposome by using 5 mg of Fb' antibody for 100 mg of lipids.**

Applicants respectfully submit that Tagawa does not teach each and every element as recited in Applicants' claims whereby the anticipation rejection is without appropriate basis. In particular, the obviousness rejection is evidence of a lack of anticipation in Tagawa because the same claims are separately rejected under 35 U.S.C. 103(a) due to difference between Applicants' claimed invention and the disclosure of Tagawa. For example, the obviousness rejection asserts that, "Tagawa's does not teach the entire claimed range of the bonded compound and the bonded antibody."



Still further, throughout Applicants' originally filed application, patentable differences are set forth over the disclosure of Tagawa. In this regard, the Examiner's attention is directed to **Applicants' specification at page 2, first full paragraph wherein Tagawa is contrasted with reference being made to the 5 mg addition of antibodies as noted above in Example 2 of Tagawa.**

Moreover, beginning in the next paragraph on page 2 of Applicants' specification and continuing through page 3, the advantages of Applicants' invention are further discussed.

The unexpected advantages of using a smaller amount of bound antibody according to Applicants' invention is also apparent from a review of Applicants' Example 4. As explained in Example 4, a smaller amount of bound antibody gives a higher therapeutic effect, and this result is unexpected by one of ordinary skill in the art in view of Tagawa which discloses the use of a larger amount of bound antibody than the presently claimed liposome, medicament composition and method.

Applicants further submit that the dependent claims are patentable over Tagawa for the reasons set forth above. Moreover, the dependent claims are patentable for the subject matter included therein in combination with their parent claims. For example, claim 11 further patentably defines that an amount of the bonded antibody is 1.2 to 2 mg per 100 mg of total lipids that constitute the liposome.

In view of the above, the anticipation and obviousness rejections should be withdrawn.

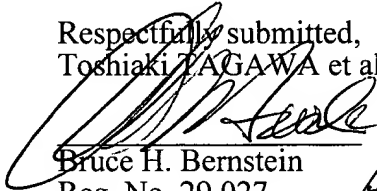
**CONCLUSION**

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow each of the pending claims.

Applicant therefore respectfully requests that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,  
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